REMARKS

In response to the Notice of Non-Responsive Amendment mailed September 13, 2005, Applicants hereby supply revised corrected pages 4,5,7, and 8. Careful examination of the other corrected pages 6 and 11 filed on June 13, 2005 indicates that they were correctly marked as then submitted.

CONCLUSION

It is believed that this application is now in condition for allowance, and action to that effect is therefore courteously requested.

Respectfully submitted,

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assay in urine, *Chest* 2001, vol. *119,* 243-9; Yu V.L., Kellog, J.A, Plouffe, J.F. *et al,* Evaluation of the Binax Urinary, Gram stain and sputum culture for *Streptococcus pneumoniae* in patients with community-acquired pneumonia, 38th Annual Meeting of the Infectious Disease Society of America, New Orleans, LA, Abstract #262 (2001).

The NOW® bioassay is described and claimed in co-pending, commonly assigned U.S. Patent Application Serial No. 09/397,110 filed September 16, 1999, which is incorporated herein by reference, and is now U.S. patent 6,824,997 issued November 30, 2004, and also in its parent application Serial No. 09/156,486 filed September 18, 1998 and now abandoned.

A study of pneumonia conducted in China found that children with nasopharyngeal carriage of *Streptococcus pneumoniae* had high rates of positive urine results in the NOW® test even when they had no pneumonic disease and that the test results accordingly did not fit the sensitivity and specificity profile established with adult subjects. A study in Gambia found that 87% of well children tested were nasopharyngeal carriers of *Streptococcus pneumoniae* and that 55% of these, or about 47% of this population, gave false positive results in the Binax NOW® test. See Adegbola, R.A., Obaro, S.K., Biney, E. and Greenwood, B.M., Evaluation of Binax NOW ® *Streptococcus pneumoniae* urinary antigen test in children in a community with a high carriage rate of pneumococcus, Pediatr. Infect. Dis. J. 2001, July; 20 (7) 718-719. See also Dowell, S.F., Garman, R.L., Liu, G., Levine, O.S. and Yang, Y.H., Evaluation of Binax NOW as assay for the detection of pneumococcal antigen in urine samples performed among pediatric patients, Clin Infect Dis. J. 2001, vol. *32*, 824-825 (2001). A similar study conducted among 210 children in Quito, Ecuador, confirmed that urine from children with nasopharyngeal carriage of *Streptococcus pneumoniae* gives a high proportion of false positive

results in the Binax NOW® test. See Hamer, D., Egas, J., Estrella, B., [[MacLood]] MacLeod, W. *et al*, 2002, an assessment of the Binax NOW *Streptococcus Pneumoniae* urinary test in children with Nasopharyngeal pneumococcal colonization, (Publication in press)

An article reviewing published studies performed on Scandinavian and Israeli children confirms that young children in these areas have a high rate of nasopharyngeal colonization, not only of *Streptococcus pnuemoniae* but also of the bacteria that are known to cause disease states that resemble pneumococcal pneumonia, including especially non-typable *Haemophilus influenzae* and *Moraxella catarrhalis* which, with *Strepococcus pneumoniae,* are the most common causes of otitis media. Among other agents that tend to colonize the nasopharynx and are causatives of both pneumonic illness clinically very similar to pneumococcal pneumonia and otitis media are *Staphylococcus aureus*, a number of other bacteria and some viruses. See Harper, M.B., Nasopharyngeal colonization with pathogens causing otitis media; how does this information help us? Pediatr Infec. Dis. J. vol. *18,* 1120-1124 (1999)

Copending, commonly assigned U.S. application Serial No. 09/518,165 filed March 1, 2002, describes and claims rapid immunochromatographic tests for detecting bacterial carbohydrate antigens in human bodily fluids, including urine.

The methodology for lessening and/or eliminating false positives in child carriers who are colonized nasopharyngeally as described herein is applicable to the modification of tests for antigens of other bacteria which tests are disclosed in copending, commonly assigned application Serial No. 09/518,165 as well as to the test for *Streptococcus pneumoniae* antigens described in copending commonly assigned application Serial No. 09/397,110, now U.S. Patent 6,824,997.

U.S. Serial No. 518,165, than the concentrations of the same antigens found in bodily fluids of children infected with pneumonic disease or otitis media.

The modified tests employ reduced concentrations of antibodies to the target bacterial antigens.

The objeetive of the modifications, which is to maintain high specificity for diseased patient samples and to improve sensitivity to those samples by screening out samples from healthy, but nasopharyngeally colonized, children which gave false positives in the standard NOW® test for *Streptococcus pneumoniae.*

DETAILED DESCRIPTION OF THE INVENTION

The NOW® bioassay for identifying the characteristic C-polysaccharide antigen of *Streptococcus pneumoniae* present in all serotypes of these bacteria,. has been demonstrated to be highly satisfactory in enabling physicians to make rapid, accurate diagnoses of a variety of *Streptococcus pneumoniae* - caused disease states in adults by coordinating carefully observed clinical symptoms with the test results. This ICT test is described and claimed in commonly assigned, copending U.S. patent application Serial No. 09/397,110 now U.S. patent 6, 824,997. U.S. application Serial No. 09/518,165, also copending and commonly assigned, discloses how to construct and perform analogous ICT bioassays which target characteristic carbohydrate antigens of other bacteria, including but by no means limited to non-typable *Haemophilus influenzae, Moraxella catarrhalis,* and *Staphylococcus aureus.*

The modifications disclosed herein of the NOW® test disclosed and claimed in U.S. Serial No. [[399,710]] 09/397,110, now U.S. Patent 6,824,997 render the test as so modified highly useful in enabling physicians to make rapid, accurate diagnoses of pneumococcal pneumonia and/or otitis media caused by *Streptococcus pneumoniae* in children, which diagnoses are based on the modified test results combined with clinical observations of the individual patients. Analogous modifications of the tests covered in U.S. Serial No. 09/518,165 render those tests as so modified very useful in enabling physicians to make rapid, accurate diagnoses of pneumonic diseases and otitis media of other bacterial origin in children, by combining the modified test results with clinical observation of individual child patients. Similar modifications may be made to any bioassay for an antigen characteristic of bacteria that tend to colonize nasopharyngeally in children and are causatives of pneumonic disease and/or otitis media, in order to improve diagnostic reliability on the assay results by diminishing or eliminating false positive results in children due to nasopharyngeal colonization.

To put the specific modified tests described in the examples of this application in perspective, a brief summary of the bioassay format described in both of the prior copending applications is provided. Succinctly, antibodies to the target bacteria are obtained by conventionally injecting a laboratory animal with the bacteria and conventionally obtaining from the animal a blood sample containing antibodies to the injected bacteria after a suitable time interval. Meanwhile, there is obtained from a culture of the same bacteria by a purification process described in the copending applications, an essentially protein-free carbohydrate antigen characteristic of these bacteria. The thus-purified antigen is coupled to a chromatographic column and the antibodies from the animal are rendered antigen-specific by